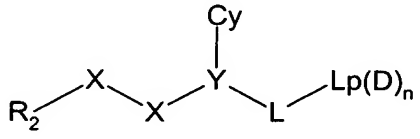
10/030188

JC03 Rec'd PCT/PTC 04 FEB 2002

Clean Set of Claims

1. (amended) A serine protease inhibitor of formula (I):



(I)

wherein:

R_2 is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachement of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, $MeSO_2$- or R_1, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R_2 cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO, CR_{1a}, $C(R_{1a})_2$ or NR_{1a} group, at least one X being C, CO, CR_{1a} or $C(R_{1a})_2$;

each R_{1a} independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R_1 is as defined for R_{1a}, provided that R_1 is not

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Sub B1

unsubstituted aminoalkyl;

Y (the α-atom) is a nitrogen atom or a CR_{1b} group;

Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group, optionally substituted by groups R_{3a} or $R_{3i}X_i$;

each R_{3a} independently is R_{1c}, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkylimidazolyl, thiazolyl, alkylthiazolyl, alkyloxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, haloalkyl, a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein X^3 is O or S; and R^{11} and R^{12} are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group), or $-OCH_2O-$ which is bonded to two adjacent ring atoms in Cy;

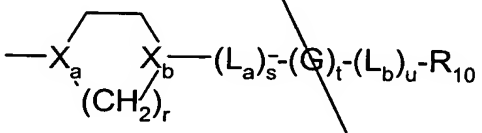
X_i is a bond, O, NH or CH_2;

R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a}; and

R_{1b}, R_{1c} and R_{1j} are as defined for R_{1a};

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

$Lp(D)_n$ is of the formula:



in which:

r is 1 or 2;

X_a is CH and X_b is N;

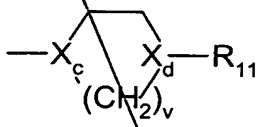
s, t and u are each 0 or 1;

L_a and L_b are each independently selected from a single bond, C=O, O and NR_{1e}, in which R_{1e} is hydrogen or (1-

6C)alkyl;

G is (1-6C)alkanediyl; and

R_{10} is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl; pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two R_3 groups [wherein R_3 is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy, or haloalkyl]}, pyrrolinyl; or a group of formula:



in which v is 1,2 or 3; one of X_c and X_d is N and the other is CH or N (provided that when v is 1, X_c and X_d are not both N); and R_{11} is hydrogen, (1-6C)alkyl or when X_d is CH, hydroxy(1-6C)alkyl; provided that when t is 0, the sum of s and u is 1; when X_b is N, L_a is a bond or C=O; when X_c is N, L_b is a bond or C=O; when X_b and X_c are both N, t is 1; and when $(L_a)_s$-$(G)_t$-$(L_b)_u$ represents an alkyl group and X_b and X_c both represent N, the alkyl group contains at least two chain carbon atoms;

or R_{10} is hydrogen and s, t and u are each 0;

contd. cl

or the compound of formula (I) that is 4-{[4-methoxybenzoyl-D,L-(2-trifluoromethylthiophenyl)-glycinyl]aminomethyl}-1-isopropylpiperidine;

but excluding the compound 4-[(3-ethoxybenzoyl-D,L-phenylglycinyl)aminomethyl]-1-[4-chlorobenzyl]piperidine;

or a physiologically-tolerable salt thereof.

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2. (amended) A serine protease inhibitor according to claim 1, wherein:

R_2 is a 5 or 6 membered aromatic carbon ring optionally interrupted by a nitrogen, oxygen or sulphur ring atom, optionally being substituted in the 3 and/or 4 position (in relation to the point of attachement of X-X) by halo, nitro, thiol, haloalkoxy, hydrazido, alkylhydrazido, amino, cyano, haloalkyl, alkylthio, alkenyl, alkynyl, acylamino, tri or difluoromethoxy, carboxy, acyloxy, $MeSO_2$- or R_1, or the substituents at the 3 or 4 positions taken together form a fused ring which is a 5 or 6 membered carbocyclic or heterocyclic ring optionally substituted by halo, haloalkoxy, haloalkyl, cyano, nitro, amino, hydrazido, alkylthio, alkenyl, alkynyl or R_{1j}, and optionally substituted in the position alpha to the X-X group (i.e. 6 position for a six membered aromatic ring etc) by amino, hydroxy, halo, alkyl, carboxy, alkoxycarbonyl, cyano, amido, aminoalkyl, alkoxy or alkylthio with the proviso that R_2 cannot be aminoisoquinolyl;

each X independently is a C, N, O or S atom or a CO, CR_{1a}, $C(R_{1a})_2$ or NR_{1a} group, at least one X being C, CO, CR_{1a} or $C(R_{1a})_2$;

each R_{1a} independently represents hydrogen or hydroxyl, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl;

R_1 is as defined for R_{1a}, provided that R_1 is not

contd. a1 sub B1

unsubstituted aminoalkyl;

Y (the α-atom) is a nitrogen atom or a CR_{1b} group;

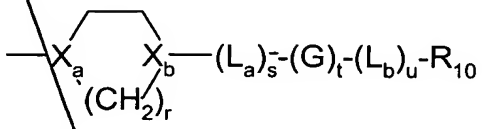
Cy is a saturated or unsaturated, mono or poly cyclic, homo or heterocyclic group optionally substituted by groups R_{3a} or phenyl optionally substituted by R_{3a};

each R_{3a} independently is R_{1c}, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl; and

R_{1b}, R_{1c} and R_{1j} are as defined for R_{1a};

L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; and

$Lp(D)_n$ is of the formula:



in which:

r is 1 or 2;

X_a is CH and X_b is N;

s, t and u are each 0 or 1;

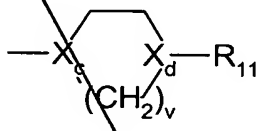
L_a and L_b are each independently selected from a single bond, C=O, O and NR_{1e}, in which R_{1e} is hydrogen or (1-6C)alkyl;

G is (1-6C)alkanediyl; and

R_{10} is (1-6C)alkyl; (3-6C)cycloalkyl [which is unsubstituted or substituted by (1-6C)alkyl]; indanyl;

contd. A1

pyridyl; tetrahydropyranyl; tetrahydrothiopyranyl; phenyl {which is unsubstituted or substituted by one or two R_3 groups [wherein R_3 is hydrogen, hydroxyl, alkoxy, alkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), hydroxyalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl, aminoalkyl (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), alkylamino (optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl or cycloalkyl), amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkysulphenyl, triazolyl, imidazolyl, tetrazolyl, hydrazido, alkyl imidazolyl, thiazolyl, alkyl thiazolyl, alkyl oxazolyl, oxazolyl, alkylsulphonamido, alkylaminosulphonyl, aminosulphonyl, haloalkoxy or haloalkyl]}, pyrrolinyl; or a group of formula:



in which v is 1, 2 or 3; one of X_c and X_d is N and the other is CH or N, provided that when v is 1, X_c and X_d are not both N; and R_{11} is hydrogen, (1-6C)alkyl or when X_d is CH, hydroxy(1-6C)alkyl; provided that when t is 0, the sum of s and u is 1; when X_b is N, L_a is a bond or C=O; when X_c is N, L_b is a bond or C=O; when X_b and X_c are both N, t is 1; and when $(L_a)_s$-$(G)_t$-$(L_b)_u$ represents and alkyl group and X_b and X_c both represent N, the alkyl group contains at least two chain carbon atoms,

or a physiologically-tolerable salt thereof.

3. (amended) A serine protease inhibitor according to claim 1, wherein R^3 is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, propyl, 2-propyl, butyl, 2-butyl, t-

contd. cl

butyl, pentyl, 2-pentyl, 3-pentyl, isopropylaminomethyl, dimethylamino-methyl, diethylaminomethyl, dimethylaminoethyl, acetyl, hydroxymethyl, hydroxyethyl, carboxy, carboxy(1-5C)alkyl, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, aminomethyl, aminocarbonyl, aminocarbonyl(1-5C)alkyl, methylamino, dimethylamino, ethylamino, formylamino, acetylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, isopropylsulphonyl, methylsulphenyl,1,2,4-triazol-2-yl, 1,2,4-triazol-4-yl, 1,2,3-triazol-4-yl, 1,3-imidazol-1-yl,1,3-imidazol-4-yl, tetrazol-1-yl, tetrazol-5-yl, methylsulphonamido, ethylsulphonamido, propylsulphonamido, methylaminosulphonyl, ethylaminosulphonyl, propylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl and trichloromethyl.

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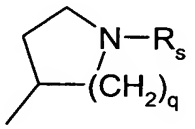
4. (amended) A compound according to claim 1 wherein r is 2.

5. A compound according to claim 1 wherein $Lp(D)_n$ is of the formula:



wherein:

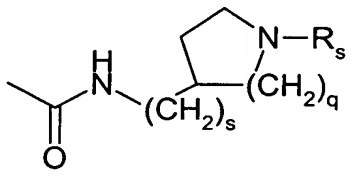
q is 1 or 2;

R_s is hydrogen, $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [c is 0, 1 or 2; wherein R_c is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and R_e and R_f are independently hydrogen or C_{1-3}alkyl; or

CHR_eR_f is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the CH group which is bonded to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

6. (amended) A compound according to claim 1 wherein L is CONH, CH_2NHCO, $CONHCH_2$, $CONHCH_2CH_2$ or $CON(Me)CH_2$.

7. A serine protease inhibitor according to claim 2 wherein -L-$Lp(D)_n$ is of the formula:



wherein

q is 1 or 2;

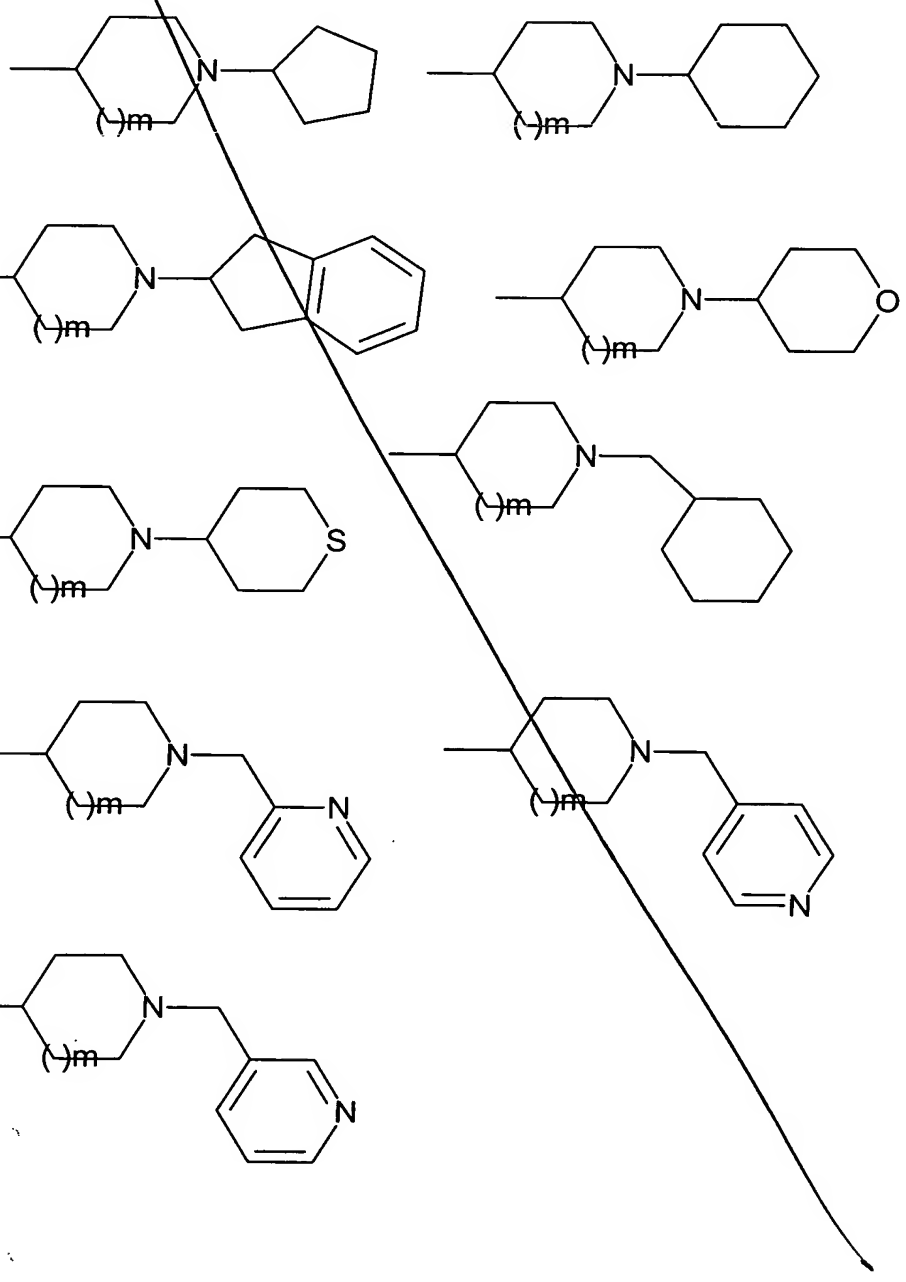
s is 0 or 1; and

R_S is $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [wherein c is 1 or 2; R_c is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and R_e and R_f are independently hydrogen or C_{1-3}alkyl; or CHR_eR_f is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or

hydroxymethyl substitutent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

8. (amended) A compound according to claim 5 wherein q is 2.

9. (amended) A compound according to claim 1 wherein $Lp(D)_n$ is selected from one of the following formulae:



contd. Q3

wherein m represents 0 or 1.

Sub B1

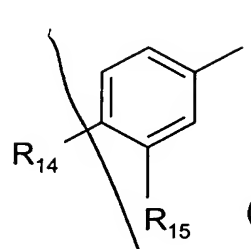
10. (amended) A compound according to claim 7 wherein R_S is selected from: hydrogen, methyl, ethyl, prop-2-yl, but-2-yl, pent-3-yl, hept-4-yl, cyclopentyl, cyclohexyl, cyclohexylmethyl, 1-methylpiperidin-4-yl, tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, phenyl, benzyl, pyrid-2-yl, pyrid-3-yl, pyrid-4-yl, pyrid-3-ylmethyl, pyrid-4-ylmethyl and indan-2-yl.

11. (amended) A compound according to claim 1 wherein R_2 is phenyl, thien-2-yl, naphthyl, indol-2-yl, indol-6-yl, benzo[b]furan-5-yl, benzo[b]thiophen-2-yl or benzimidazol-2-yl (each of which is optionally substituted as defined in claim 1).

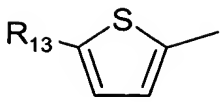
12. (amended) A compound according to claim 11 wherein optional substituents for R_2 are selected from: fluoro, chloro, bromo, iodo, nitro, thiol, difluoromethoxy, trifluoromethoxy, hydrazido, methylhydrazido, amino, cyano, trifluoromethyl, methylthio, vinyl, ethynyl, acetylamino, carboxy, acetoxy, hydroxy, methyl, ethyl, amido ($CONH_2$), aminomethyl, methoxy and ethoxy.

13. (amended) A compound according to claim 1 wherein R_2 is selected from one of the formula (A') to (H'):

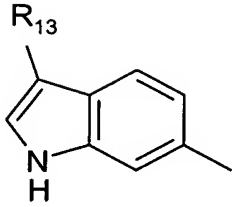
contd. A3



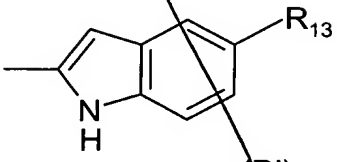
(A')



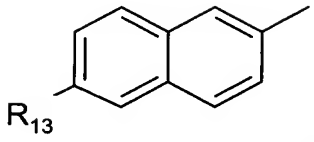
(B')



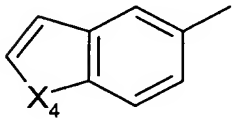
(C')



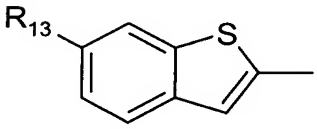
(D')



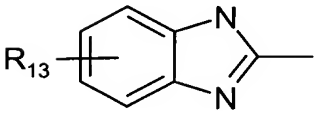
(E')



(F')



(G')



(H')

wherein X_4 is O or S, R_{13} is selected from hydrogen, fluoro, chloro or methyl and R_{14} is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and R_{15} is selected from hydrogen, methyl, fluoro, chloro and amino.

14. (amended) A compound according to claim 1, wherein R_2 is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl.

15. (amended) A compound according to claim 1 wherein -X-X- is -CONH-.

contd. Q3 16. (amended) A compound according to any one of claims 1 to 15, 17 to 18 and 21 to 24 wherein Y is CH.

17. (amended) A compound according to claim 1 wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl, furanyl, pyrrolyl, isoxazolyl, isothiazolyl, pyrazolyl, oxazolyl, imidazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, pyrimidinyl, pridazinyl, quinolyl, isoquinolyl, benzofuryl, benzothienyl or cycloalkyl group, or a phenyl group substituted by $R_{3i}X_i$ in which X_i is a bond, O, NH or CH_2 and R_{3i} is phenyl, pyridyl or pyrimidinyl optionally substituted by R_{3a}.

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18. (amended) A compound according to claim 1 wherein Cy is an optionally R_{3a} substituted: phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group.

19. (cancelled on national phase entry)

20. (cancelled on national phase entry)

Q4 21. (amended) A compound according to claim 1 wherein R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, CH_2CONH_2, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, bromo, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy, trifluoromethyl, pyrrolidin-1-ylcarbonyl,

Sub B1

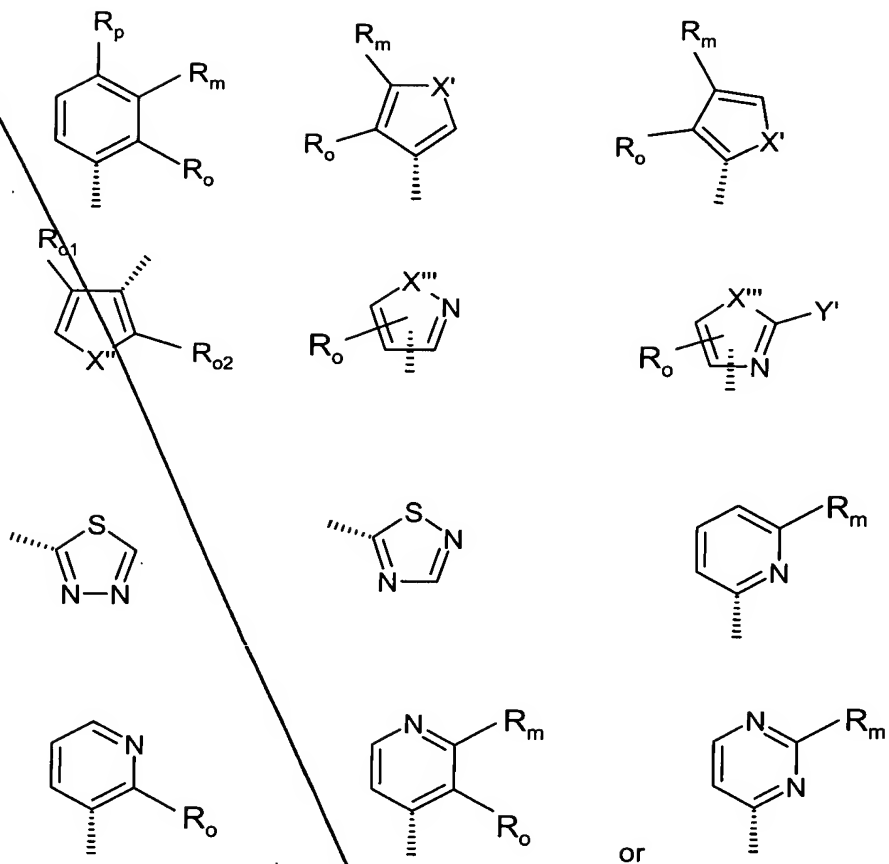
contd. cl 4

piperidin-1-ylcarbonyl, morpholin-1-ylcarbonyl and $-OCH_2O-$ (which is bonded to two adjacent ring atoms in Cy).

22. (amended) A compound according to claim 1 wherein R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy, methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, CH_2CONH_2, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl.

23. (amended) A compound according to claim 1 wherein Cy is selected from:

contd. cl 4



Sub B1

wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

R_o is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

R_m is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl, methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein X^3 is O or S and R^{11} and R^{12} are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

R_p is selected from hydrogen and fluoro; or

contd. Q4

R_o and R_m or R_m and R_p form an $-OCH_2O-$ group; or R_o and R_m together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroary ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of R_{o1} and R_{o2} is hydrogen and the other is R_o.

Sub B1

24. (amended) A compound according to claim 1 wherein Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-3-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, naphthyl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-4-yl, quinolin-5-yl, and quinolin-8-yl.

25. (amended) A compound as claimed in Claim 16, in which the alpha atom in Y is carbon and has the conformation that would result from construction from a D-α-aminoacid $NH_2-CR_{1b}(Cy)-COOH$ where the NH_2 represents part of X-X

26. (amended) A pharmaceutical composition, which comprises a compound as claimed in claim 1 together with at least one pharmaceutically acceptable carrier or excipient.

27. (cancelled on national phase entry).

28. (cancelled on national phase entry).

Q5 Sub B1

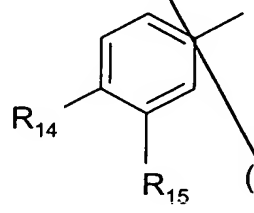
29. (amended) A method of treatment of a human or non-human animal body to combat a thrombotic disorder, which comprises administering to said body an effective amount of a compound as claimed in claim 1, but including the compound 4-[(3-ethoxybenzoyl-D,L-phenylglycinyl)aminomethyl]-1-[4-chlorobenzyl]piperidine.

30. (cancelled on national phase entry).

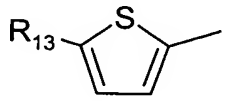
31. (cancelled on national phase entry).

32. (New) A compound according to Claim 1 wherein:

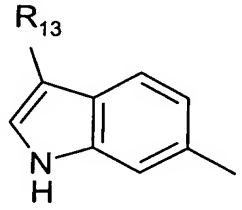
R_2 is is selected from one of the formula (A') to (H'):



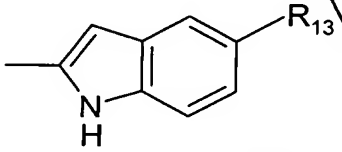
(A')



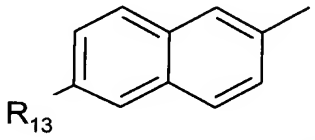
(B')



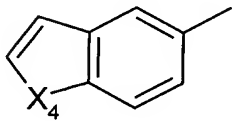
(C')



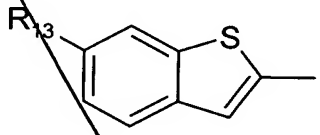
(D')



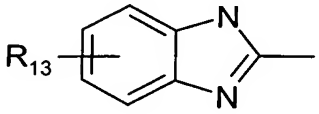
(E')



(F')



(G')



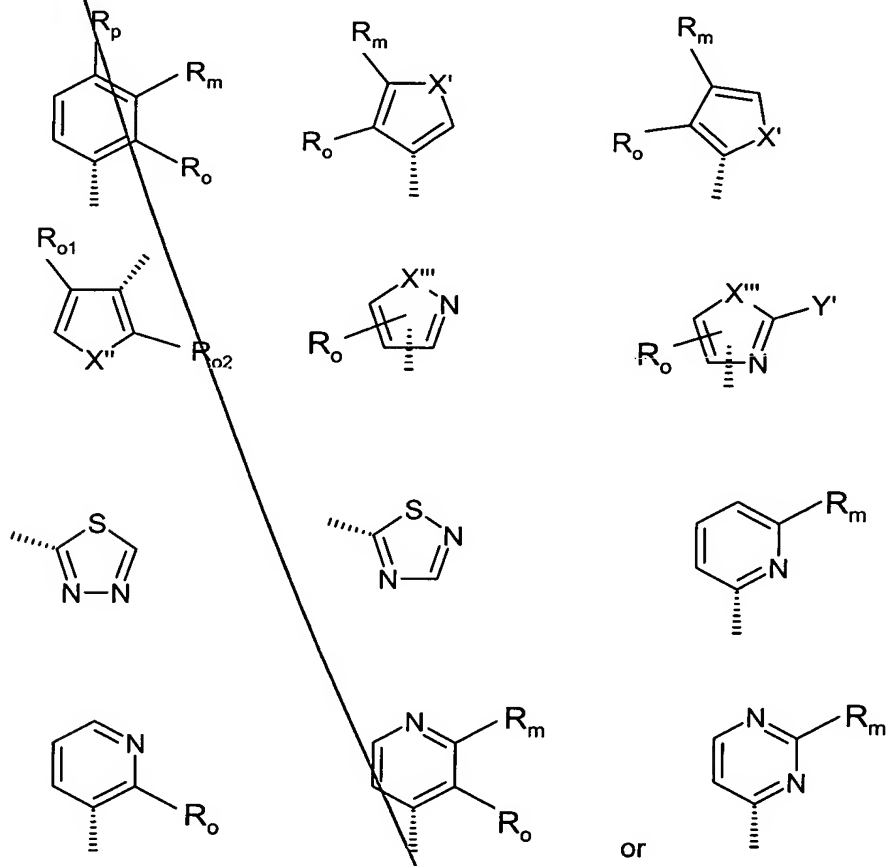
(H')

wherein X_4 is O or S, R_{13} is selected from hydrogen, fluoro, chloro or methyl and R_{14} is selected from hydrogen, methyl, ethyl, fluoro, chloro, and methoxy and R_{15} is selected from hydrogen, methyl, fluoro, chloro and amino;

X-X represents CONH;

contd. Y (the α-atom) is CH and has the conformation that would result from construction from a D-α-aminoacid NH_2-CR_{1b}(Cy)-COOH where the NH_2 represents part of X-X;

Cy is selected from:



or

wherein:

X' is selected from O, S and NMe;

X'' is selected from O and S;

X''' is selected from O, S, NH and NMe;

Y' is selected from hydrogen, amino and methyl;

R_O is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl and methylsulphonyl;

R_m is selected from hydrogen, methyl, fluoro, chloro, trifluoromethyl, methoxy, methylthio, methylsulphinyl,

contd. Cl 6

methylsulphonyl, carboxy, methoxycarbonyl and a group of the formula $-C(X^3)N(R^{11})R^{12}$ (wherein X^3 is O or S and R^{11} and R^{12} are independently selected from hydrogen, methyl or ethyl or together with the nitrogen atom to which they are attached form a pyrrolidin-1-yl, piperidin-1-yl or morpholino group);

R_p is selected from hydrogen and fluoro; or

R_o and R_m or R_m and R_p form an $-OCH_2O-$ group; or

R_o and R_m together with the ring to which they are attached form a 5 or 6 membered aryl or heteroaryl ring (wherein the heteroary ring contains 1 or 2 heteroatoms selected from nitrogen, oxygen and sulfur);

one of R_{o1} and R_{o2} is hydrogen and the other is R_o; and

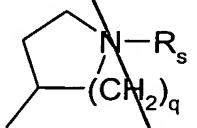
L is CONH, CH_2NHCO, $CONHCH_2$, $CONHCH_2CH_2$ or $CON(Me)CH_2$.

33. (New) A compound according to Claim 32 wherein

R_2 is 4-methoxyphenyl, 3-amino-4-chlorophenyl, indol-2-yl, 5-chloroindol-2-yl, indol-6-yl, 3-chloroindol-6-yl or 3-methylindol-6-yl;

Cy is selected from phenyl, 2-chlorophenyl, 2-methoxyphenyl, 4-carbamoylphenyl, pyrid-2-yl, pyrid-3-yl, thien-2-yl, thien-3-yl, furan-2-yl, furan-3-yl, imidazol-2-yl, thiazol-2-yl, thiazol-4-yl, thiazol-5-yl, naphthyl, isoquinolin-5-yl, isoquinolin-8-yl, quinolin-4-yl, quinolin-5-yl, and quinolin-8-yl; and

$Lp(D)_n$ is of the formula:



wherein:

q is 1 or 2;

R_s is hydrogen, $-(CH_2)_c-R_c$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [c is 0, 1 or 2; wherein R_c is pyridyl or phenyl (which phenyl may

contd. Cl 6

bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and R_e and R_f are independently hydrogen or C_{1-3}alkyl; or CHR_eR_f is (3-6C)cycloalkyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position, provided the substituent is not bonded to the CH group which is bonded to L), tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl (which may bear a 1-methyl substituent), piperidinyl (which may bear a 1-methyl substituent) (provided that the tetrahydropyranyl, tetrahydrothiopyranyl, pyrrolidinyl and piperidinyl rings are not linked to the piperidin-1,4-diyl group through a ring nitrogen atom or a ring carbon atom adjacent to a ring oxygen, sulfur or nitrogen atom) or indan-2-yl].

Sub B1

34. (New) A compound according to Claim 2 wherein

R_2 represents:

(i) phenyl optionally being substituted in the 3 and/or 4 position by fluoro, chloro, bromo, iodo, nitro, difluoromethoxy, trifluoromethoxy, amino, cyano, trifluoromethyl, methylthio, vinyl, carboxy, acetoxy, $MeSO_2$-, hydroxy, methoxy, ethoxy, methyl, methoxycarbonyl, methylamino, ethylamino or amido, and optionally substituted at the 6 position by amino, hydroxy, fluoro, methoxycarbonyl, cyano or aminomethyl;

(ii) naphth-2-yl optionally substituted at the 6, position by hydroxy and optionally substituted at the 3 position by amino or hydroxy;

(iii) isoquinolin-7-yl, indol-5-yl, indol-6-yl, indazol-5-yl, indazol-6-yl, benzothiazol-6-yl or benzisoxazol-5-yl optionally substituted at the 3 position by chloro, bromo, amino, methyl or methoxy;

contd. A6

(iv) benzimidazol-5-yl or benzothiazol-6-yl optionally substituted at the 2 position by amino;

(v) thien-2-yl or thien-3-yl optionally substituted at the 4 or 5 position by methylthio, methyl or acetyl;

(vi) 3,4-methylenedioxyphenyl, 2,3-dihydroindol-6-yl, 3,3-dichloro-2-oxo-indol-6-yl or 1-methyl-3-aminoindazol-5-yl;

Sub B1

(vii) benzothiazol-2-yl, imidazo[1,2-a]pyrimidin-2-yl or tetrahydroimidazo[1,2-a]pyrimidin-2-yl;

(viii) pyrazol-2-yl substituted at the 5 position by methyl;

(ix) pyrid-2-yl optionally substituted at the 6 position by chloro;

(x) pyrid-3-yl optionally substituted at the 4 position by chloro;

(xi) benzofur-2-yl optionally substituted at the 3 position by chloro, methyl or methoxy, at the 5 or 6 position by methyl and at the 6 position by methoxy;

(xii) indol-2-yl optionally substituted on the indole nitrogen atom by methyl and optionally substituted at the 5 or 6 position by fluoro, chloro, bromo, methyl or methoxy;

(xiii) indol-6-yl substituted at the 5 position by chloro, fluoro or hydroxy and optionally substituted at the 3 position by chloro or methyl; or

(xiv) benzo[b]thiophen-2-yl optionally substituted at the 3 position by fluoro, chloro or methyl, and optionally substituted at the 5 or 6 position by fluoro, chloro, methyl, hydroxy, or methoxy;

X-X represents CONH;

Y (the α-atom) is CH and has the conformation that would result from construction from a D-α-aminoacid NH_2-CR_{1b}(Cy)-COOH where the NH_2 represents part of X-X;

Cy is an optionally R_{3a} substituted phenyl, pyridyl, thienyl, thiazolyl, naphthyl, piperidinyl or cycloalkyl group;

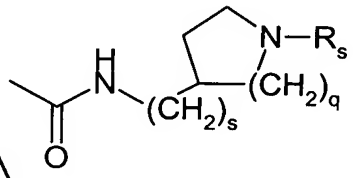
R_{3a} is selected from hydrogen, hydroxyl, methoxy, ethoxy,

contd. cl 6

methyl, ethyl, methylaminomethyl, dimethylaminomethyl, hydroxymethyl, carboxy, methoxymethyl, methoxycarbonyl, ethoxycarbonyl, methylaminocarbonyl, dimethylamino-carbonyl, aminomethyl, $CONH_2$, CH_2CONH_2, acetylamino, methoxycarbonylamino, ethoxycarbonylamino, t-butoxycarbonylamino, amino, fluoro, chloro, cyano, nitro, thiol, methylthio, methylsulphonyl, ethylsulphonyl, methylsulphenyl, methylsulphonylamido, ethylsulphonylamido, methylaminosulphonyl, ethylaminosulphonyl, aminosulphonyl, trifluoromethoxy and trifluoromethyl; and

Sub cl

$-L-Lp(D)_n$ is of the formula:



wherein

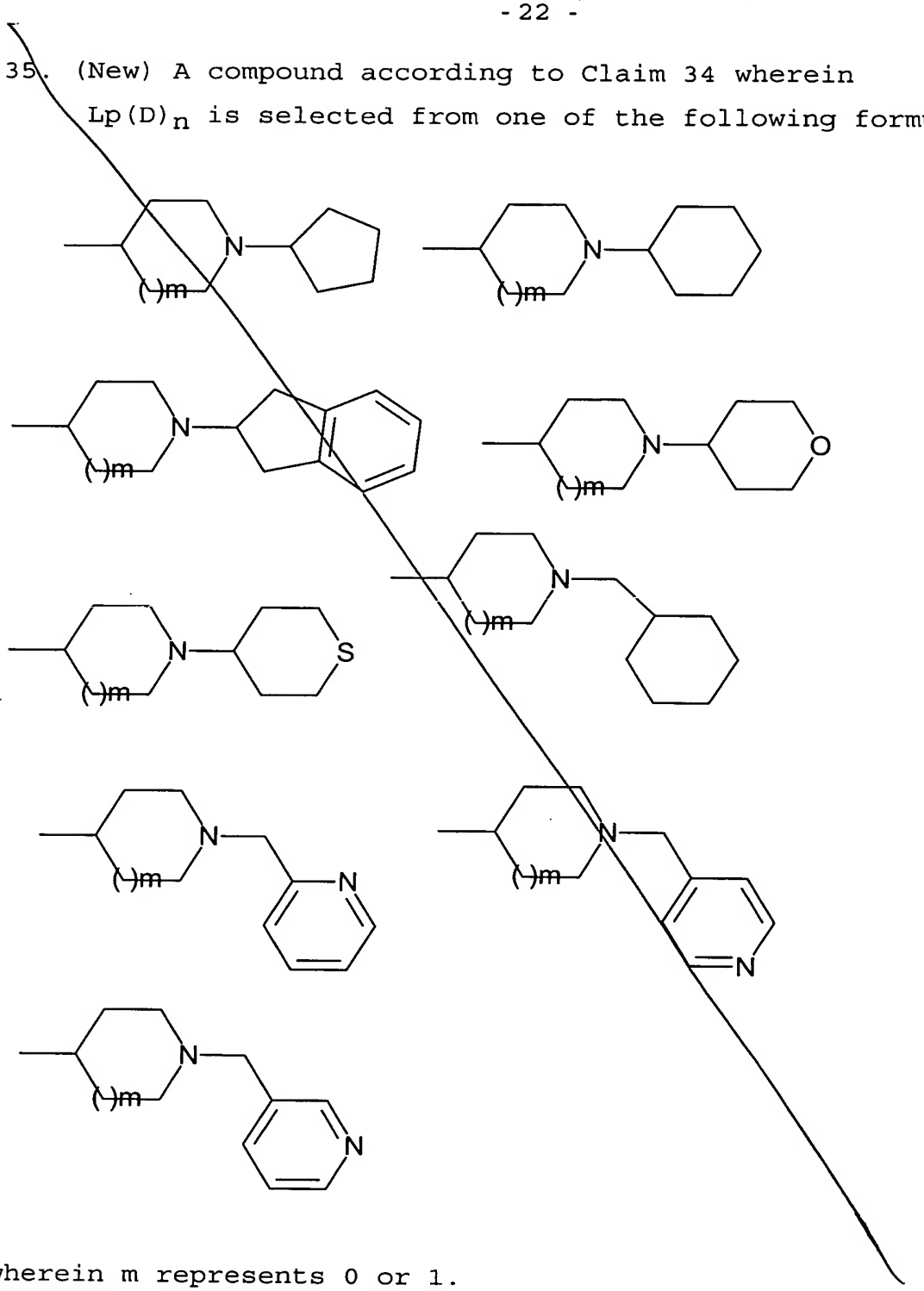
q is 1 or 2;

s is 0 or 1; and

R_S is $-(CH_2)_c-R_C$, $-CHR_eR_f$, or $-CH_2-CHR_eR_f$ [wherein c is 1 or 2; R_C is pyridyl or phenyl (which phenyl may bear a fluoro, chloro, methyl, $CONH_2$, SO_2NH_2, methylaminosulphonyl, dimethylaminosulphonyl, methylsulphonylamino, methoxy or methylsulphonyl substituent) and R_e and R_f are independently hydrogen or C_{1-3}alkyl; or CHR_eR_f is cyclopentyl (which may bear a methyl, ethyl or hydroxymethyl substituent at the 3- or 4-position), cyclohexyl (which may bear a methyl, ethyl or hydroxymethyl substitutent at the 3- or 4-position), tetrahydropyran-4-yl, tetrahydrothiopyran-4-yl, pyrrolidin-3-yl (which may bear a 1-methyl substituent), piperidin-4-yl (which may bear a 1-methyl substituent), or indan-2-yl].

contd. 6

35. (New) A compound according to Claim 34 wherein $Lp(D)_n$ is selected from one of the following formulae:



wherein m represents 0 or 1.